REMARKS

Claims 6-21 have been cancelled as directed to a non-elected inventions. Claim 1 has been amended to insert the limitations of claim 4. Claim 4 has been cancelled as redundant. No new matter has been added and entry of the amendment is respectfully requested.

Claim 1-3 were objected as obvious over Little *et al.*; this basis for rejection is obviated by the amendment to claim 1 as claims 4 and 5 were not included in this basis for rejection.

The only other ground for rejection was of claims 1-5 over the combination of Little *et al.* in view of Kim *et al.* or Hayakawa *et al.*. This basis for rejection is respectfully traversed.

Little is cited under 35 U.S.C. §103/102(e) as suggesting that agents that inhibit mitochondrial ATP synthase also are antiproliferative agents. There is no suggestion in Little, however, that the chances of finding a suitable compound in a screen for ATP synthase inhibitors could be improved by choosing as the candidate compounds analogs of apoptolidin. Accordingly, the Office cites Kim and Hiyakawa based on their disclosure, as set forth on page 1 of the application, that apoptolidin is an antiproliferative agent. The Office reasons that because apoptolidin is an antiproliferative agent, it therefore follows that selection among its analogs for use as antiproliferative agents could be effected by screening for ability to inhibit mitochondrial ATP synthase.

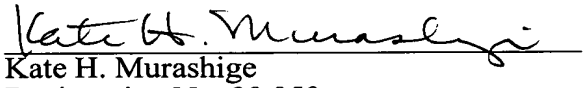
Respectfully, this logic does not follow. It is not true that if all inhibitors of mitochondrial ATP synthase are antiproliferative agents that therefore all antiproliferative agents inhibit mitochondrial ATP synthase. It is this latter proposition that must be true in order to make the claimed subject matter obvious. It is not until applicants have demonstrated that apoptolidin and its analogs employ inhibition of ATP synthase as a means to inhibit proliferation

(as opposed to some other mechanism) that it becomes clear that this assay can be used to identify which among them are antiproliferative agents. This is the contribution of the invention itself; there is no suggestion in the art that apoptolidin and its analogs are useful candidate compounds for this type of screening.

Accordingly, it is believed that this basis may properly be withdrawn and claims 1-3 and 5 passed to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 286002021220.

Respectfully submitted,

Dated: May 5, 2003 By: 

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